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(54) METHOD OF VALIDATING MRNA SPLCIING MUTATIONS IN COMPLETE TRANSCRIPTOMES

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(57) **ABSTRACT**

A method is described for the automatic validation of DNA sequencing variants that alter mRNA splicing from nucleic acids isolated from a patient or tissue sample. Evidence the a predicted splicing mutation is demonstrated by performing statistically valid comparisons between sequence read counts of abnormal RNA species in mutant versus non-mutant tissues. The method leverages large numbers of control samples to corroborate the consequences of predicted splicing variants in complete genomes and exomes for individuals carrying such mutations. Because the method examines all transcript evidence in a genome, it is not necessary a priori to know which gene or genes carry a splicing mutation.